REMARKS

In view of the foregoing amendments and the following representations, reconsideration and allowance of the above-identified application is respectfully requested.

Claims 35, 37, 39, 40, 42, 44 and 47-51 are pending in the present application. Claims 1-34, 36, 38, 41, 43 and 45-46 have been canceled without prejudice.

On page 8 of the Office Action, the Examiner objected to claim 35 because the second to last line contained a typographical error. In response to this objection, Applicants have amended claim 35 to correct the typographical error.

On page 8 of the Office Action, the Examiner rejected claims 35-46 under 35 U.S.C. § 103(a) as being unpatentable over the teachings of Cutie et al., WO 01/82875 ("Cutie") in view of Lewis, WO 01/35940 ("Lewis") and further in view of Vergez et al., United States Published Patent Application No. 2006/0204578 ("Vergez").

Although Applicants do not agree with this rejection, in an effort to expedite prosecution of the present application, Applicants have amended independent claim 35 and present new independent claim 47 which recite a particular embodiment of the present invention. Support for the amendments and newly presented claims can be found on page 7, lines 8-15 (description of the semipermeable membrane); page 10, line 20 to page 11, line 20 (description of the weight percentages); and Example 6 on page 22, line 9 to page 25, line 14.

The pending claims recite a specific once a day metformin tablet consisting of a controlled release metformin core prepared with specific excipients to control the release

of the metformin in a specific manner and an immediate release pioglitazone coating applied to a primary seal coat surrounding the controlled release metformin core.

The pending claims also require the controlled release core to contain only one active ingredient, metformin hydrochloride, and a specific semipermeable membrane surrounding the core to control the release of the metformin. The claims also require a primary seal coat that is applied to the semipermeable membrane of the controlled release metformin core and onto which the immediate release pioglitazone coating is applied. As stated in the prior submissions, Applicants discovered after much research that the use of a primary seal coat allowed the successful application of an immediate release pioglitazone coating to a semipermeable metformin coating.

Applicants respectfully submit the pending claims are patentable over the cited references because the combination of the references would not lead a skilled artisan to prepare a metformin/pioglitazone tablet as recited in the pending claims.

The Examiner contends that Cutie discloses a "core formulation comprising a first layer comprising pioglitazone, which covers at least a portion of a core comprising the biguanide, metformin (i.e. glucophage)". March 13, 2009 Office Action, Page 9-10. The Examiner also states that the core formulation of Cutie "may be coated with sugar, shellac or other enteric coating agents (Page 7, lines 9-11)" and "can have an outer shell made of a biodegradable material (including cellulosic polymers, polyvinyl acetate, and polyvinyl alcohol) (Page 7, lines 13-28)". March 13, 2009 Office Action, Page 10.

The Applicants do not dispute that Cutie teaches applying a pioglitazone layer to a metformin core, however, Applicants respectfully submit Cutie does not disclose or

suggest coating the metformin core with a modified release coating and applying an immediate release pioglitazone coating to a seal coated modified release metformin core. Applicants respectfully submit that the Examiner is incorrectly interchanging the terms "core" and "core formulation" as used in Cutie. Cutie defines "core formulation" as a combination of a metformin core with a pioglitazone coating. For example, Page 1, lines 6-8 of Cutie states:

> This invention relates to a **core formulation**, and, more particularly, to a **core formulation** comprising a first layer comprising pioglitazone, which covers at least a portion of a **core** comprising the biguanide, metformin (i.e., glucophage).

(emphasis added).

Similarly, Page 3, lines 3-6 of Cutie states:

> The first layer of the core comprises pioglitazone hydrochloride in an amount of 0.01% to 20% of the **total weight of the core formulation**, whereas, the metformin in the core is present in an amount of 10% to 97.5% of the **total weight of the core formulation**.

(emphasis added).

See also: Page 6, lines 17-18 of Cutie (wherein it is stated "The resultant core formulation of the present invention is useful to treat diabetes mellitus") and Claim 1 (which describes the "core formulation" as containing both the metformin and the pioglitazone).

Clearly, Cutie defines the "core formulation" as containing both metformin and pioglitazone. Therefore, when Cutie states the "core formulation of the present invention may be coated with sugar, shellac or other enteric coating agents", Cutie is instructing the skilled artisan to coat both the metformin and pioglitazone with these coatings. This

description is consistent with the teachings on Page 8, lines 6-14 wherein an embodiment of Cutie is described as the core formulation with the first layer encapsulated by a shell to provide a delayed release of the metformin and pioglitazone. *See also*: Claim 7 of Cutie which describes a method for forming a controlled release dosage form that comprises inserting a metformin and pioglitazone into a shell.

Applicants respectfully submit that Cutie does not disclose a once a day tablet as recited in the present claims because the teachings of Cutie direct a skilled artisan to prepare a "core formulation" comprising both metformin and pioglitazone and applying the modified release coating to the combined "core formulation".

The addition of Lewis and/or Vergez does not overcome the deficiencies of Cutie. In fact, Vergez merely confirms and motivates a skilled artisan to follow the teachings of Cutie and prepare a dosage form wherein both the metformin and pioglitazone are in a modified release form.

Specifically, Vergez teaches a "dual controlled release dosage form" wherein the dosage form contains at least two active ingredients that are released in a controlled manner. *See generally:* Vergez ¶¶ 2, 15 and 22. Vergez describes a number of ways in which to prepare the dual controlled release dosage but never discloses or suggests a dosage form wherein one of the active ingredients is released immediately as required by the pending claims.

Applicants do not believe a skilled artisan would combine Vergez with Cutie, however, if such a combination were undertaken, Applicants respectfully submit the resulting combination would result in a dosage form wherein both the metformin and

pioglitazone are released in a controlled manner and not a dosage form wherein the metformin is released in a controlled manner and the pioglitazone in an immediate release manner as required by the pending claims.

The addition of Lewis to either the Cutie and/or Vergez references would not lead the skilled artisan to the presently claimed invention. As described previously, Lewis teaches an immediate release dosage form containing immediate release forms of both metformin and pioglitazone. There is no mention, disclosure or suggestion of preparing a controlled release metformin core and an immediate release pioglitazone layer as required by the pending claims. At best, Lewis teaches the metformin and pioglitazone components should be separated by an inert barrier. This teaching of Lewis, when added to Cutie, merely suggests to the skilled artisan that the metformin and pioglitazone components should be separated by an inert layer; it does not motivate or lead a skilled artisan to modify the teachings of Cutie and remove the pioglitazone component from the core of the "core formulation". Even if the skilled artisan were to depart from the teachings of Cutie and prepare a tablet with an immediate release pioglitazone layer, the teachings of Lewis would not direct or motivate a skilled artisan to arrive at the presently claimed invention which requires a semipermeable membrane and a primary seal coating between the metformin core and pioglitazone.

The addition of Lewis to Cutie and Vergez would similarly not direct a skilled artisan to the presently claimed invention. The combination of Lewis, Cutie and Vergez would lead a skilled artisan to prepare a core consisting of a metformin component and a pioglitazone component separated by an inert barrier layer. This core would then be

coated with a modified release coating. This proposed structure that a skilled artisan should obtain by combining the Lewis, Cutie and Vergez references is very different from the single controlled release structure recited in the pending claims which requires controlled release of the metformin, immediate release of the pioglitazone and a semipermeable membrane and primary seal coat separating the metformin and pioglitazone.

On page 16 of the Office Action, the Examiner maintained the provisional non-statutory obviousness-type double patenting rejection of claims based upon co-pending Application No. 11/094,493. As indicated in the December 29, 2008 submission, Applicants respectfully request this rejection be held in abeyance pending the finding of allowable subject matter in either the present application or Application No. 11/094,493. Once allowable subject matter is found in either application, Applicants will consider submitting a terminal disclaimer if appropriate.

Based upon the foregoing amendments and representations, Applicants respectfully requested that the rejection of the claims in the above-identified application be withdrawn. Early and favorable action is earnestly solicited.

Respectfully submitted,

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